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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,099	08/08/2001	Yoshihiro Nishida	NISHIDA=3A	3370

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,099	NISHIDA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 11, filed on 15 July 2003 is acknowledged and entered. Following the amendment, the original claims 1-46 are canceled, and the new claims 47-50 are added.

Currently, claims 47-50 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 14, 15, 18, 19, 37 and 38 are moot as the applicant has canceled the claims.

Formal Matters:

The amended title of the invention is still not descriptive. A title should be more specific and clearly indicative of the claimed invention. "Method of treatment using anti-IL-18 antibody" is suggested.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 is indefinite for the recitation of "does not completely contain the amino acid sequences of the constant regions" in lines 10-11. It is unclear whether such a limitation encompasses peptides that do not contain the amino acid sequences of the constant regions, or if they contain some amino acid sequences of the constant regions (and if so, which sequences). The metes and bounds of the claim, therefore, cannot be determined. Claims 48-50 are similarly indefinite.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi et al. (J Immunol. Methods, 1997, 206: 107-113, provided by applicants), in view of Kohno et al. (Clin. Immunol. Immunopath., January 1998, 86(1): 11-15), and Riechmann et al. (Nature, 1988, 332:323-327).

The teachings of Taniguchi and Kohno are reviewed in the last Office Action, paper No. 10, at page 5. Briefly, Taniguchi discloses a mouse anit-human IL-18 monoclonal antibody, #125-2H, which is identical to that of the instant application, and capable of neutralizing IL-18, and Kohno teaches methods of administering anti-IL-18 antibodies for treating a pathological condition, and pathological role of IL-18 in diseases such as autoimmune insulitis and diabetes, and rheumatoid arthritis (RA).

Neither reference teaches explicitly a method to treat a disease such as RA using a composition comprising a peptide for neutralizing IL-18, wherein the peptide comprises variable regions of an IL-18 antibody and does not completely contain the constant regions of said antibody.

Riechmann teaches a method to make a humanized antibody (see page 325-327 of the reference). A humanized antibody allows an antibody generated from a non-human origin to retain the specificity and biological effects of the original antibody but have the potential to be nonimmunogenic in humans. The effector functions of such a chimaeric antibody can be selected or tailored. Additionally, the use of human isotypes minimize the anti-globulin response during therapy by avoiding anti-idiotypic antibodies (see page 323 of the reference).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the antibody disclosed by Taniguchi to a humanized antibody to obtain the known and expected advantages such as those taught by Riechmann. Such antibody would meet the limitation of the present claims as being a peptide for neutralizing IL-18, comprising variable regions of the IL-18 antibody, and not completely containing the constant regions of said antibody. The person of ordinary skill in the art would have been motivated to make a humanized IL-18 antibody using the monoclonal antibody taught by Taniguchi, and to use such an antibody for the treatment of diseases or inflammatory conditions such as RA as suggested by Kohno since Taniguchi's antibody is an *anti-human* IL-18 antibody, and it would be suitable for treating those human diseases, and reasonably would have expected success because Riechmann has successfully demonstrated such humanized antibody.

Claims 47-50 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi et al. (J Immunol. Methods, 1997, 206: 107-113, provided by applicants), in view of Kohno et al. (Clin. Immunol. Immunopath., January 1998, 86(1): 11-15), and Huston et al. (Proc. Natl. Acad. Sci., 1988, 85(16):5879-83).

The teachings of Taniguchi and Kohno are reviewed in the last Office Action, paper No. 10, at page 5, and summarized above.

Neither reference teaches explicitly a method to treat a disease such as RA using a composition comprises a peptide for neutralizing IL-18, wherein the peptide comprises variable regions of an IL-18 antibody and does not completely contain the constant regions of said antibody.

Huston teaches a method of constructing an anti-digoxin single chain antibody fragment, scFv (see page 5879-80, and Figure 2 of the reference), which retained the antigen binding activity and specificity of the parent antibody. As known in the art, scFv is one approach to stabilizing the Fv fragments in bacteria. The main advantages of scFv are the rapid clearance from human circulation and reduced toxic side effects (Sandhu, 1992, Critical Reviews in Biotech., 12(5/6): 437-462, especially page 450, F).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the antibody disclosed by Taniguchi to make a scFv antibody fragment for the known advantages of such as reduced toxic side effects. Such antibody fragment would meet the limitation of the present claims as being a peptide for neutralizing IL-18, comprising variable regions of the IL-18 antibody, and not completely containing the constant regions of said antibody. The person of ordinary skill in the art would have been motivated to make a humanized IL-18 antibody using the monoclonal antibody taught by Taniguchi, and to use such an antibody for the treatment of diseases or inflammatory conditions such as RA as suggested by Kohno since Taniguchi's antibody is an *anti-human* IL-18 antibody, and it would be suitable for treating those human diseases, and reasonably would have expected success because Huston has successfully demonstrated such antibody fragment.

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
8/18/03